REMARKS

The Official Action of 28 February 2006 has been carefully considered and reconsideration of the application as amended is respectfully requested.

Claims 11-15 and 23 have been canceled whereby to render moot the rejections under 35 USC 112, first paragraph appearing at paragraph 3 (Written Description) and paragraph 4 (Enablement) of the Official Action.

The sole rejection remaining is the rejection under 35 USC 103 for alleged unpatentability over Nordiff in view of Paliwal et al and Puri et al. Applicants respectfully traverse this rejection.

Each of the claims under rejection is directed to a method for inhibiting transmission of malaria by the administration of **a single dose** of the claimed compound to an animal. The invention defined by these claims is based upon Applicants' discovery that a single dose of the claimed compound within the recited amount has gametocytocidal activity. In particular, the experimentation described in the specification at pages 14-15 and Table I on page 18 shows that the claimed compound kills gametocytes of *P. cynomolgi* within erythrocytes in blood of Rhesus monkeys when the recited compound is administered in a single dose in any of the claimed amounts within a seven day period (see Table I on page 18 of the specification). The specification also shows that the monkeys were not infective even after the seven day period shown in Table I (see specification at page 15, first full paragraph).

The Examiner states that the cited art teaches the claimed method except for the recited dosage/regimen of the claimed compound, but this is respectfully believed to be inaccurate and based upon a faulty premise: inhibiting the transmission of malaria by administering an effective amount of CDR1 80/53 was **not** known in the prior art. As discussed next, the prior art does not provide one of skill in the art with even a reasonable expectation that the claimed compound would be effective in a method for inhibiting the transmission of malaria as claimed.

The primary reference, Nodiff et al describes two test systems: (i) blood schizontoicidal test trophozoite induced P. berghei infection in mice, and (ii) radical curative (antirelapse) test for tissue stages in liver of Rhesus monkeys (P. cynomolgi bastianelli strain sporozoite induced infection) Primaquine 1.00 mg/kg free base x 7 days in combination with chloroquine. The Nordiff et al teachings are based on the above two tests with a categorical statement that the invention therein is restricted to a "method for treating malaria caused by the presence of malaria parasites in the blood, formed tissues, or blood and formed tissues, which comprises the step of administering parenterally or orally to an infected animal an antimalarial effective amount of a compound....." Nordiff et al do not disclose or teach or guide towards gametocytocidal activity/transmission blocking action and does not contain any experimental data on this activity.

In any event, it is respectfully erroneous to presume that all primaquine derivatives possess gametocytocidal activity. Coleman et al (1992, Am. J. Trop Med. Hyg. 46: 169-182) clearly state that WR 242511 is also an 8-aminoquinoline but does not have any gametocytocidal/sporontocidal activity (Coleman et al at page 176 of reference). This clearly

shows that the effectiveness of the claimed invention (where the novelty resides in gametocytocidal activity) could not have been expected from Nordiff et al.

Similarly, Paliwal et al and Puri et al do not disclose or predict or teach towards or even guide towards gametocytoxidal action. Puri et al teach activity against tissue stage of parasites (hypnozoites) after sporozoite induced infection for which the radical curative dose is disclosed as being 1.2mg/kg x 7 days. This again is based on Rhesus monkey model. The antirelapse activity of Puri et al and the activity of the claimed invention are radically different and are aimed at different stages in the parasite life cycle. Antirelapse activity refers to killing of tissue stage in liver while transmission blocking action refers to sterilization of gametocytes which fail to infect malaria vector in Anopheles mosquito.

In view of the above, Applicants respectfully submit that the cited art does not provide even a reasonable expectation of success with the claimed method and thus cannot set forth even a *prima facie* case of obviousness for the invention as claimed for this reason alone (see MPEP 706.02(j)). Moreover, the cited art cannot set forth even a *prima facie* case because it does not show or suggest the claimed dosages/regimen and thus does not show all of the claim limitations.

As discussed above, the claimed method is a method for **inhibiting transmission of malaria** and the claimed dosages thus refer to gametocytocidal activity of the claimed compound which blocks transmission of sexual stages of Plasmodia through mosquito vector.

The only prior art cited that shows the claimed compound teaches against tissue stages where 1.25 mg/kg x 7 days produces a curative response (see discussion above). The cited art does not show effectiveness of the claimed compound for inhibiting transmission of malaria, and thus does not show the claimed method.

The Examiner cites case law and MPEP 2144.05 to the effect that, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover optimum or workable ranges by routine experimentation. But this authority is respectfully not applicable in the present case where the general conditions of the present claims- -inhibiting the transmission of malaria- -are **not** disclosed in the prior art and the discovery is not just of optimum or workable ranges, but of a different method. Indeed, it is respectfully submitted that one cannot optimize a range where one does not know what the optimization is for. With respect to the cited art, any optimization would be with respect to antirelapse or radical curative activity, not gametocytocidal activity.

In short, each compound has to be evaluated independently in animal models to establish its profile as a causal prophylactic, blood schizontocidal, radical curative or gametocytocidal compound. The prior art does not show with even a reasonable expectation of success that the claimed compound can be used as a gametocytocidal compound and thus does not set forth even a *prima facie* case of obviousness for the invention as claimed.

In view of the above, it is respectfully submitted that all rejections and objections of record have been overcome and that the application is now in allowable form. An early notice of allowance is earnestly solicited and is believed to be fully warranted.

Respectfully submitted,

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